## SDC Table 2: Studies Included with Pacemaker (CRT)

<table>
<thead>
<tr>
<th>Study</th>
<th>Design/Sample</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Results</th>
<th>Summary/Conclusions</th>
</tr>
</thead>
</table>
| Greco et al      | **Design:** Single group; Pre/post (n=11)                                     | **EX:** Formal or informal aerobic training program, (3-5 d/wk at aerobic workloads (30-45min) at home or in outpatient setting | **4 mo:** Exercise capacity  
- Peak VO₂ (mL/kg/min)  
- Anaerobic threshold time (ATT) min  
- Exercise time (ET) min | **4 mo:** Exercise capacity  
- Peak VO₂  
Pre: 20.54±7.69  
Post: 25.32±10.97  
P=.002  
ATT  
Pre: 6.86±2.24  
Post: 13.18±4.22  
P<.001  
ET  
Pre: 11.50±2.73  
Post:17.14±5.14  
P<.001  
Adverse events  
Not reported (NR) | Level of Evidence: VI  
Jadad score = NR  
**Strength**  
- Tailoring of CPET was done for the type of rate response pacemaker  
**Weakness**  
- Small sample size  
- Not all exercise programs were the same, some were done at home and others supervised  
- Not all follow-up times were at the same time following training. |
<table>
<thead>
<tr>
<th>Design: prospective RCT (n=8) who got exercise, matched to CRT no exercise (n=9), compared to historical controls (n=19) who got no exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample: patients with LV systolic dysfunction and LBBB, cardiac resynchronization therapy CRT and dyssynchrony 1 month after CRT implanted, EF&lt;35%,</td>
</tr>
<tr>
<td>CRT device: Guidant CRT-P= 13 Guidant CRT-D=4 Settings in DDD mode</td>
</tr>
<tr>
<td>Gender (M/F): CRT group CRT+: 3/5 CRT-: 5/4 C group HF+:7/2</td>
</tr>
<tr>
<td>Conraads et al (2007)22</td>
</tr>
</tbody>
</table>

### Exercise

- **EX:** Supervised ambulatory endurance exercise program 1h x 3x/wk x 4 mo at HR 90% of the ventilatory threshold. (n=17)
- **CRT+** Standard pharmacological therapy plus 4-mo endurance exercise training program with CRT (n=8)
- **HF+** Standard pharmacological treatment plus 4-mo endurance exercise training- no CRT (n=9)

### 5 mo:

- **Exercise capacity**
  - Peak VO₂ (mL/kg/min)
  - Peak Watts (maximal workload (wattmax)

- **LV remodeling**
  - LVEF
  - Left ventricular end-diastolic (LVEDD)
  - Left ventricular end-systolic diameter (LVESD)

- **QOL**
  - MLHFQ

- **Biomarker**
  - NT-pro brain natriuretic peptide (NT-proBNP)

<table>
<thead>
<tr>
<th>5 mo: Exercise capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO₂</td>
</tr>
<tr>
<td>CRT+: 19.3±1.2</td>
</tr>
<tr>
<td>CRT- : 13.8 ±0.9</td>
</tr>
<tr>
<td>P=.005</td>
</tr>
<tr>
<td>Watt peak</td>
</tr>
<tr>
<td>CRT+: 113±12</td>
</tr>
<tr>
<td>CRT- : 87 ±9</td>
</tr>
<tr>
<td>P=0.0005</td>
</tr>
<tr>
<td>LV remodeling</td>
</tr>
<tr>
<td>LVEF</td>
</tr>
<tr>
<td>CRT+: 36±5</td>
</tr>
<tr>
<td>CRT- : 34 ± 6</td>
</tr>
<tr>
<td>P=.50</td>
</tr>
<tr>
<td>LVEDD</td>
</tr>
<tr>
<td>CRT+: 59+3</td>
</tr>
<tr>
<td>CRT- : 68 ± 4</td>
</tr>
<tr>
<td>P=.30</td>
</tr>
<tr>
<td>LVESD</td>
</tr>
<tr>
<td>CRT+: 47±3</td>
</tr>
<tr>
<td>CRT- : 54±5</td>
</tr>
<tr>
<td>P=.30</td>
</tr>
<tr>
<td>QOL</td>
</tr>
<tr>
<td>MLHFQ</td>
</tr>
<tr>
<td>CRT+: 30±6</td>
</tr>
</tbody>
</table>

**Level of Evidence: II**

**Jadad score = 3**

**Strength**

- 4 group design
- 2 historical group controls used with no CRT

**Limitations**

- Small patient groups - relative short follow-up time
- There are no comparisons done between those with CRT who exercised and HF patients without CRT who exercised, to determine the benefits of exercise and CRT.
<table>
<thead>
<tr>
<th>Design:</th>
<th>prospective RCT (n=50) 3 mo after CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groups:</td>
<td>NYHA functional class III to IV who received CRT, QRS&gt;120 msec, LVEF%&lt;35%,</td>
</tr>
<tr>
<td>Gender %:</td>
<td>M: 92%</td>
</tr>
<tr>
<td>Age (mean):</td>
<td>64.4y</td>
</tr>
</tbody>
</table>

**Age (mean ± SD)**
- **CRT group**
  - CRT+: 57±2
  - CRT-: 61±4
- **C group**
  - HF+: 65±3
  - HF-: 64±4

**LVEF (mean ± SD):**
- **CRT group**
  - CRT+: 27±5
  - CRT-: 28±5
- **C group**
  - HF+: 28±3
  - HF-: 26±2

**Dropout rate:**
- NR

**HF–:** standard pharmacological treatment no CRT (n=10)

**Biomarker**
- NT-proBNP
  - CRT+: 1698±802
  - CRT-: 711±198
  - P=.70

**Adverse events**
- No lead dislodgement
- Normal LV thresholds

**Patwala et al (2009)**

<table>
<thead>
<tr>
<th>6 mo:</th>
<th>Exercise capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO2</td>
<td>EX: 20.10±3.84</td>
</tr>
<tr>
<td>C: 18.07±3.89</td>
<td></td>
</tr>
<tr>
<td>P=.02</td>
<td></td>
</tr>
</tbody>
</table>

**Peak cardiac power output (CPO)**
- Maximum RER %Peak VO2 at the anaerobic threshold

**Echocardiogram**
- Left ventricular end-diastolic

**Level of Evidence:** II
**JADAD=3**

**Strength:**
- Randomization delayed to determine effects of CRT alone until the 3 mo
- Exercise training in a nonclinical setting and by using a physician not involved in the pacemaker implant or follow up
<table>
<thead>
<tr>
<th>Smolis-Bąk et al (2015)&lt;sup&gt;3&lt;/sup&gt;</th>
<th><strong>Design:</strong> prospective randomized observation (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample</strong></td>
<td>HF of ischemic or another etiology, NYHA class III</td>
</tr>
<tr>
<td><strong>Gender:</strong></td>
<td>% (n): Male: EX=96.1% C=84.6%</td>
</tr>
</tbody>
</table>

| **EX:**  | Initial aerobic exercise training in the hospital setting (3 wk) and continued training program at home with telemonitoring. Large and small muscle isometric exercises, respiratory exercises, ROM exercises both in hospital and at home up to 3 mo; n=26. |

<table>
<thead>
<tr>
<th><strong>4 mo:</strong></th>
<th><strong>Exercise capacity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak VO&lt;sub&gt;2&lt;/sub&gt; (ml/kg/min)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Exercise time (min)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>METs</strong></td>
<td></td>
</tr>
<tr>
<td><strong>6MWD (meters)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>QOL</strong></td>
<td>NHP-EL NHP-LM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>4 mo:</strong></th>
<th><strong>Exercise capacity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PeakVO&lt;sub&gt;2&lt;/sub&gt;</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Ex time</strong></td>
<td></td>
</tr>
<tr>
<td><strong>METs</strong></td>
<td></td>
</tr>
<tr>
<td><strong>6MWD</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Weakness:</strong></th>
<th>- Relatively small sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Control group not receiving CRT but randomized to exercise training would have improved the methodology</td>
</tr>
</tbody>
</table>

| **Adverse events** | NR |

| **Level of Evidence:** | II |

| **Jadad score** | =1 |

<table>
<thead>
<tr>
<th><strong>Strengths</strong></th>
<th>- 12 mo follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Home telemonitoring used to monitor safety while exercising at home</td>
</tr>
</tbody>
</table>

| **Limitations** | - No aerobic exercise training provided |
| **Age** | 62±9.3y  
EX: 60±8.5y  
C: 65.1±8.2y |
| **CRT device** | CRT-D |
| **Disease** | Ischemic cardiomyopathy  
EX=42.6%  
C=50% |
| **LVEF% (mean ± SD)** | EX: 25.3±7.4  
C:24.9±7.2 |
| **C: Hospital rehabilitation (3 wk), but no training program after discharge (n=26)** |
| **Depression** | Beck Depression Inventory  
12 mo: Same as 4 mo |
| **Echocardiogram** | - Left ventricular end-diastolic dimension-LVDD  
- Left ventricular end systolic dimension-LVSD  
- LVEF |
| **6MWD** | EX=460±99  
C=435±107  
P=NR |
| **QOL** | NHP-EL  
EX: 1±0.8  
C:1.2±1.0  
P=.43 |
| | NHP-LM  
EX:1.5±1.2  
C:2.3±1.4  
P=.03 |
| **Depression** | BDI  
EX: 10.3±6.9  
C: 12.0±7.3  
P=.41 |
| **Exercise capacity** | PeakVO₂  
EX: 13.1±4.1  
C:14.2±3.1  
P=.94 |
| | Time  
EX: 7.34±3.07  
C:5.42±3.09  
P=.38 |
<table>
<thead>
<tr>
<th></th>
<th>Ex.</th>
<th>C.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>METs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>5.74±2.22</td>
<td>4.62±2.38</td>
<td>.61</td>
</tr>
<tr>
<td><strong>6MWD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>466±113</td>
<td>456±108</td>
<td>NS</td>
</tr>
<tr>
<td><strong>QOL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHP-EL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>0.9±0.8</td>
<td>1.2±0.9</td>
<td>.14</td>
</tr>
<tr>
<td>NHP-LM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>1.2±1.1</td>
<td>2.0±1.5</td>
<td>.03</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>8.3±5.7</td>
<td>11.9±5.9</td>
<td>.12</td>
</tr>
<tr>
<td><strong>Echocardiogram</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVDD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>6.53±0.97</td>
<td>6.41±1.07</td>
<td>.70</td>
</tr>
<tr>
<td>LVSD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EX:</td>
<td>4.48±1.28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Zeitler et al (2015)\textsuperscript{50} | **Design:** prospective RCT | **EX:** Supervised cardiac rehab 18 sessions 40 min 5x per wk, at 60% to 70% of heart rate reserve, followed by home exercise 5x/wk 40 min 60-70% of HRR for 9 mo; n=1149 | **3 mo:**  
**Exercise Capacity**  
Exercise time (min)  
Peak VO\(_2\) (mL/kg/min)  
**QOL**  
KCCQ  
**Pro BNP**  
**Adverse Events:** All cause mortality  
Composite of CV death or CV hospitalization  
Composite of CV health or HF hospitalization | **3 mo:**  
**Exercise Capacity**  
Peak VO\(_2\)  
ICD  
EX: 15.1  
C: 14.5  
CRT-D  
EX: 14.9  
C: 13.9  
No device  
EX= 15.9  
C=15.6  
P=NS  
**Exercise time**  
ICD  
EX: 10.8  
C: 9.8  
CRT-D  
EX: 10.6  
C:9.3  
No device | **Level of Evidence:** II  
**Jadad score** = 3  
**Strengths**  
- Largest HF exercise trial completed to date  
**Limitations**  
- Not blinded to collection of outcome data  
- Complete data not reported, no mean±SD data, no P values.  
- Considerable missing data |
| --- | --- | --- | --- | --- | --- |
| **Sample** (n=1118)  
Outpatients with HF and LVEF ≤35%. NYHA 2-4, with implanted ICD or CRT device  
Comparison group = no device (n=1200) | **CRT Device:**  
- ICD: single and dual-chamber ICD (n=683)  
- Biventricular lead: CRT-D (n=435)  
**Gender:** n(%)  
Female 430(35%)  
RV=137 (20%)  
CRT-D 94 (22%)  
**Age:** 58y  
ICD = 61y |  
**C:** No restricted activity  
n=1160  
  
**LVEF**  
EX: 28.9±9.1  
C: 31.7±10.6  
P=.33  
**Adverse events**  
NR |  
**C:** 4.78±1.15  
P=.47 |
| CRT-D=61 y | | EX 11.6  
| C=10.5  
P=NS  

| Ethnicity  
AA 483 (40%)  
ICD 173(20%)  
CRT-D 93(22%)  

| Diagnosis  
Ischemic cardiomyopathy  
n=512 (42%)  
ICD 456( 67%)  
CRT-D 229 (53%)  

| LVEF 25±21.31  
ICD 24%  
CRT-D 23%  

| Dropout rate:  
No device 19.9%  
ICD: 15.1%  
CRT-D: 17.1%  

| KCCQ total  
RV lead  
EX: 73  
C: 72  

| CRT-D  
EX:72  
C:71  

| No device  
EX=69  
C=70  
P=NS  

| Pro-BNP  
RV lead  
EX: 998.2  
C: 959.8  

| CRT-D  
EX: 1197  
C: 881.5  

| No device  
EX=480.8  
C=558  
P=NS  

| Difference among device groups:  
**All cause mortality**  
P=.33 |
**Final List: Pacemaker**

Total: 5 Studies

| All cause death or hospitalization | P=.06 |
| CV death or CV hospitalization     | P=.19 |
| Hospitalization rates             | Higher for those with devices vs no device, 26% vs 15% |
| Adverse events                    | NR |


Table abbreviations: AV, atrioventricular; BDI, Beck Depression Inventory; C, control group; CPET, cardiopulmonary exercise test; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization-defibrillator; CRT-P, cardiac resynchronization-pacemaker; CRT+, with cardiac resynchronization therapy; CRT-, no cardiac resynchronization therapy; CPR, cardiopulmonary resuscitation; CV, cardiovascular; EF, ejection fraction; EX, exercise intervention; f/u, follow-up; HF, heart failure; HF+, with heart failure; HF-, no heart failure; HR, heart rate; ICD, implantable cardioverter defibrillator; KCCQ, Kansas City Cardiomyopathy Questionnaire; LV, left ventricular; LVEF, left ventricular ejection fraction; METs, metabolic equivalents; MLHFQ, Minnesota Living with Heart Failure Questionnaire; NHP-EL, Nottingham Health Profile-Energy Level; NHP-LM, Nottingham Health Profile-Limited Mobility; NYHA, New York Heart Association; NR, not reported; QOL, quality of life; RCT, randomized controlled trial; RV, right ventricle; SD, standard deviation; VO₂, oxygen uptake; 6MWD, 6-minute walk distance.